REMARKS

Claims 17, 25 to 27 and 29 to 32 are pending in the instant application. Claims 17 and 29 have been amended by deleting reference to treating viral or bacterial infections and inflammatory diseases and deleting the reference to the corresponding cells in step (a), thereby directing the claimed invention to the treatment of a tumor. Furthermore, for the sake of clarity, the tumor to be treated has been characterized to comprise tumor cells which express Hsp70 on their cell surface. Support for this amendment may be found throughout the specification as filed, for example at page 1, lines 13–14; page 11, lines 18–20 in conjunction with page 13, lines 4–6 as well as in the Examples.

In the Office Action mailed December 29, 2008, the Examiner rejected the claims under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement because, according to the Examiner, the claims contained subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant respectfully disagrees. However, in an effort to advance prosecution, and not in acquiescence to the Examiner's objection, applicants have amended claims 17 and 29 by drawing the claimed invention to treating a tumor comprising tumor cells which bear Hsp70 on their cell surface. Accordingly, the Examiner's objections concerning the alleged missing guidance as to how one would extrapolate the teaching of the specification to treating viral or bacterial infections or inflammatory diseases are rendered moot.

With respect to the Examiner's objection that the specification fails to provide sufficient guidance as to how one would induce apoptosis in the absence of an essential co-factor, such as perforin, applicant respectfully disagrees. In particular, the Examiner relies on publications by Shi (Shi, et al. J. Exp. Med. (1997) 185(5), pages 855-866; IDS 10/12/07) and Trapani (Trapani and Sutton. Curr. Opin. Immunol. (2003) 15, pages 533 – 543) stating that the specification of the present application fails to provide guidance as to how one would overcome the art recognition that granzyme B enters cells in the absence of perforin, yet does not induce apoptosis until perforin in *[sic]* administered. *See* Office Action at 5, second paragraph.

However, applicant submits that at the time of two mentioned publications, the present invention was not yet known in the art. Applicant herewith submits the publication by Gross et al., J. Biol. Chem. 42 (2003), 41173 – 41181, co-authored by the present inventor in which the

experiments on which the claimed invention is based have been published in a peer-reviewed journal. As stated, for example, in the abstract of the Gross publication and by accepting the manuscript for publication acknowledged in the art:

> "Incubation of tumor cells with increasing concentrations of perforin-free, isolated granzyme B shows specific binding and uptake in a dose-dependent manner and results in initiation of apoptosis selectivity in tumor cells presenting Hsp70 on the cell surface"

See Gross at page 1173, left column (emphasis added)."

The same teaching is to be found in the specification and the claims, *i.e.*, that the tumor cells of the tumor to be treated express Hsp70 on their cell surface. *See also* examples 3 and 4 as well as figures 3 and 4 demonstrating that exogenously provided granzyme B enters selectively Hsp70 membrane-positive tumor cells and induces apoptosis in the absence of perforin. Thus, the specification provides sufficient guidance as to how one would induce apoptosis in the absence of perforin, since according to the present invention, and as demonstrated in the examples and reflected in claims 17 and 29, Hsp70 on the cell surface of the tumor cells represents the "essential co-factor" for doing so.

Since, as demonstrated, the essential co-factor is represented by Hsp70 on the cell surface of the target tumor cells, it is also submitted that the nature of the tumor, for example colon or any other source is irrelevant as to the practicability of the claimed invention. Rather, as stated in the Gross publication "a novel perforin-independent, granzyme B-mediated apoptosis pathway for Hsp70 membrane-positive tumor cells" is provided. *See* Gross at page 4, 1173, left column, last sentence of the abstract.

Accordingly, applicant respectfully submits that with the amendment and the above explanations, the basis for the previous rejection has been overcome.

Conclusion

The Applicant believes the arguments set forth above traverse the Examiner's rejections and therefore request these alleged grounds for objection and rejection be withdrawn. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned collect.

Dated: March 26, 2009

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